3R Research Foundation Switzerland

Annual Report 2017

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3R-Principles

The 3Rs are Replace, Reduce and Refine animal experimentation. The 3Rs must be the guiding principles behind animal experimentation; if a study can be carried out without using any laboratory animals then such a procedure must be used (Replace). If it is essential to use laboratory animals under the terms of animal protection legislation the number used must be kept to a strict minimum (Reduce). The third "R" requires that animals used for laboratory experiments be made to suffer an absolute minimum of pain and/or stress (Refine). The 3R Research Foundation funds research projects whose aim is to improve present-day experimental methods from the point of view of the 3Rs.

The 3R Research Foundation in 2017

In 2017 the Foundation provided a total of CHF 304,156.80 for 11 research projects that had been approved previously. The Administrative Board received the final reports for four completed projects. No new applications were approved owing to the fact that the Foundation now has funding only for ongoing projects. The Foundation will receive no more funding from the federal authorities or Interpharma.

Consequently the Foundation's activities were limited mainly to transferring funds to ongoing projects.

The Administrative Board

The Administrative Board of the Foundation is made up of nine members, two representing the Swiss parliament, two representing animal protection, two from Interpharma and two from the Federal Food Safety and Veterinary Office, as well as one representative of other interested circles. Current members are:

Joachim Eder
member of the Council of States, Unterägeri
Chairman
Dr. Peter Bossard
Horw, Deputy Chairman
Dr. Philippe Bugnon
Institute of Laboratory Animal Science, University of Zurich
Dr. Isabelle Chevalley
member of the National Council, St-George
Dr. Kaspar Jörger
Federal Food Safety and Veterinary Office, Berne-Liebefeld
Dr. Ingrid Kohler
Federal Food Safety and Veterinary Office, Berne-Liebefeld
Dr. Birgit Ledermann
Novartis Pharma Ltd, Basle
Claudia Mertens
biologist, Zurich Animal Protection Leage, Winterthur
Nathalie Stieger
economist, F. Hoffmann-La Roche Ltd, Basle

The Evaluation Committee

Prof. Ernst B. Hunziker
University Hospital, Berne, Chairman
Prof. Hans Acha-Orbea
Department of Biochemistry, University of Lausanne
Dr. Franziska Boess
F. Hoffmann-La Roche Ltd, Basle
Dr. Urban Deutsch
Theodor-Kocher-Institute, University of Berne
Prof. Robert R. Friis
University of Berne
Prof. Andrew Hemphill
Institute of Parasitology, University of Berne
Dr. Ingrid Kohler
Federal Food Safety and Veterinary Office, Berne-Liebefeld
Dr. Kurt Lingenhöhl
Novartis Pharma Ltd, Basle
Prof. Matthias Lutolf
Lausanne Federal Institute of Technology
Prof. Thomas Lutz
Institute of Veterinary Physiology, University of Zurich
Prof. Alex Odermatt
Department of Pharmaceutical Sciences, University of Basle
Prof. Tatiana Petrova
University of Lausanne
Prof. Barbara Rothen-Rutishauser
Adolphe Merkle Institute, University of Fribourg
Dr. Stefanie Schindler
Animalfree Research Foundation, Berne

Scientific Adviser

Prof. Ernst B. Hunziker
University Hospital, Berne

Administrator

Ernst P. Diener, lawyer, Münsingen

Auditors

DieWirtschaftsprüfer.ch AG, Thun

Supervisory body

Federal Department of Home Affairs

Articles and statutes of the Foundation

- Deed of foundation dated 13 February 1987, modified on 28 September 2011
- Regulations dated 30 March 2011 (latest update 4 December 2014)
- Guidelines for awarding research grants dated 15 May 1987 (latest update 4 December 2014)

Summary of the Year's Activities

The Foundation's website

Detailed information about all the Foundation's activities can be found on its website at www.forschung3r.ch.

Eleven projects subsidised

A total amount of CHF 304,156.80 was paid out for 11 ongoing projects during 2017

Four projects successfully completed

In-vitro engineering of a human cell-based three-dimensional dynamic model of atherosclerosis (135/15) Dr. Benedikt Weber, Swiss Centre for Regenerative Medicine, University Hospital Zurich. The most common cause of death among people in the western hemisphere is cardiovascular disease. In the majority of cases, the causes of the disease can be traced back to lesions in the arterial cell walls, so-called atherosclerotic plaque. At present, various animal models are used to investigate the origin of cardiovascular disease as well as for developing and testing new medication aimed at preventing/arresting or even curing the disease.

In this project, the research team have succeeded in developing a three-dimensional cell culture system from human atherosclerotic plaque (from material obtained following heart and blood vessel surgery) whereby the variety of cells involved in the disease are included in the model. The system is also capable of imitating the pulsatile blood vessel phenomena for simulating the biomechanical forces that play an important role in the origin of cardiovascular disease. This system provides a new biological "tool" for this vast research field that will help to avoid the necessity of using a large number of laboratory animals. (http://www.forschung3r.ch/en/projects/pr_135_13.html)

A new in-vitro vascular model mimicking the endothelial barrier (139/14) Dr. Marietta Herrmann, AO Research Institute, Davos. Blood vessel walls, which are lined with endothelial cells that in turn are covered with pericytes, control the transport of various substances (nutrients, gases such as oxygen, etc.) in both directions (from the blood to tissue cells and vice versa). Cells also pass through this wall, e.g. antibody cells, as they spread from the blood into tissue to eliminate invasive pathogens. Until now it has not been possible to simulate this barrier function in vitro. For this reason, many experiments involving laboratory animals (mice, rats, etc.) are still being carried out in order to assess the expected barrier effect on new active substances or the extent to which antibodies can penetrate the endothelial barrier.

The successful creation of a comprehensive in-vitro blood vessel model including pericytes would provide a new research tool that would obviate the need for many experiments involving laboratory animals. The aim of this project was to create such an in-vitro system (micro-fluid chamber, basal membrane system, pericytes, etc.). Unfortunately, the technical difficulties encountered by the research team proved so extreme that they were unable to achieve their aim. Nevertheless, by designing a new modified chamber model, they did succeed in solving some of their basic problems, for example, the inclusion of air bubbles and various points of leakage in the complicated set-up. (http://www.forschung3r.ch/en/projects/pr_139_14.html)

Hydrocephalus simulator for testing active ventriculoperitoneal shunts (140/14) Dr. Marianne Schmid Daners, Institute for Dynamic Systems and Control, ETH Zurich. The ventriculoperitoneal shunts that are used in medicine today to treat hydrocephalus were developed in the 1950s. They drain brain fluid that cannot drain naturally (or be recirculated) into the abdomen. Passive pressure valves are used in these shunts that often become blocked and consequently lead to various complications. New systems are normally tested on laboratory animals.

In order to avoid such testing on animals, a new platform has been developed that consists of a simulator whereby ventriculoperitoneal shunts can be tested in vitro. The laboratory run by the leader of this project plans to build such simulators independently at first. The simulators will then be made available to scientists working at universities. (http://www.forschung3r.ch/en/projects/pr_140_14.html)

In-vitro alternatives to in-vivo bioconcentration-testing in fish: restricted to rainbow trout or broadly applicable? (141/14) Prof. Helmut Segner, Centre for Fish and Wildlife Health, Vetsuisse Faculty, University of Berne. Throughout the world there are programmes for regulating the use of chemicals such as pesticides and for estimating the risk of persistence, toxicity and accumulation, in particular bioaccumulation, in live animals. One of the most frequently used models for such evaluations concerns bioaccumulation in fish, namely in their liver cells. High numbers of laboratory fish are required for such tests. New alternative testing methods to in-vivo measurements in fish include in-vitro and in-silico methods using liver cell systems from rainbow trout, a cold-water fish.

In this project the research team succeeded in demonstrating that the data obtained from rainbow trout material (liver cells) could be reproduced using material from carp (which is often used in such tests in Asian countries). With this method it should be possible to replace animal testing totally or at least partially. The data obtained represent a major step towards the acceptance of an animal-free approach to determining the predictive bioaccumulation of chemicals in fish for the purposes of regulation in the future. (http://www.forschung3r.ch/en/projects/pr_141_14.html)

3R-Info Bulletins

No new 3R-Info Bulletins were published in 2017.

The 3R-Info Bulletins are available on the Internet (www.forschung3r.ch/en/publications/index.html)

Background of the Foundation

The Foundation is a cooperative institution set up by the Parliamentary Group for Animal Experimentation Questions (public organ), Interpharma (association of pharmaceutical companies that carry out research in Switzerland; http://www.interpharma.ch/thema/uber-interpharma) and the Animalfree Research Foundation (animal protection). The Foundation was entered in the commercial register on 18 August, 1987.

The funds for subsidising research are provided principally by the Federal Food Safety and Veterinary Office as well as Interpharma.

Purpose of the Foundation

The purpose of the 3R Research Foundation Switzerland is to promote alternative research methods through grants for research projects as well as to implement and promote the 3R principles. The organisation supports first and foremost projects aimed at developing new methods or refining accepted methods (validation) which offer improvements vis-à-vis standard animal experimentation in line with the 3R motto, Replace, Reduce, Refine

A broad range of projects is funded on the condition that they are likely to replace animal experimentation or to reduce the number of animals used or the stress and/or pain suffered. Accordingly, projects based on the Foundation's three principles and covering any of a broad selection of bio-medical disciplines will be taken into consideration.

In 2017 the Foundation approved no new projects, since it received funding from the federal authorities and Interpharma for the last time in 2016 for ensuring that ongoing projects could be completed. In the future, funding from these two sources will be made available to the new 3R Competence Centre that was founded in 2018 under the auspices of "swissuniversities". The 3R Research Foundation will therefore cease its activities and be disbanded in 2018 as soon as the ongoing projects have been completed.

Activities during 2017

In the Foundation's thirty-first year of existence the Administrative Board met twice, namely in April and December, for a half-day meeting. Apart from the statutory business concerning the end of the business year 2016, the Board addressed the following issues.

In April, the Board focused on the financial statements for 2016 and earmarking research funds for ongoing projects. In addition, it took note of the final reports on three completed projects.

At the December meeting, the Administrative Board was given a progress report on the creation of the 3R Competence Centre and received the final report on one project. Since, in view of its current aims and activities there is no future for the 3R Research Foundation, the Administrative Board decided to dissolve the Foundation once its obligations in relation to research grants have been fulfilled. The existing funds should suffice to meet all current obligations. The meeting finished with a review of activities during 2017 and those planned for 2018, which was followed by way of a thank-you for the work carried out in 2017 by a dinner for the whole Board.

In view of the decision not to call for any further applications, the Evaluation Committee did not meet during 2017. The Scientific Advisor organised the review of the annual reports and final reports by mail. We should like to take this opportunity to thank the members of the Evaluation Committee for their voluntary work in this connection.

During 2017 four projects were completed (135/13, 139/14, 140/14 and 141/14). Together with those projects completed earlier, this brings the total of finished projects to 138 out of 146

Personnel

In 2017 there were no changes in the Administrative Board nor the Evaluation Committee.

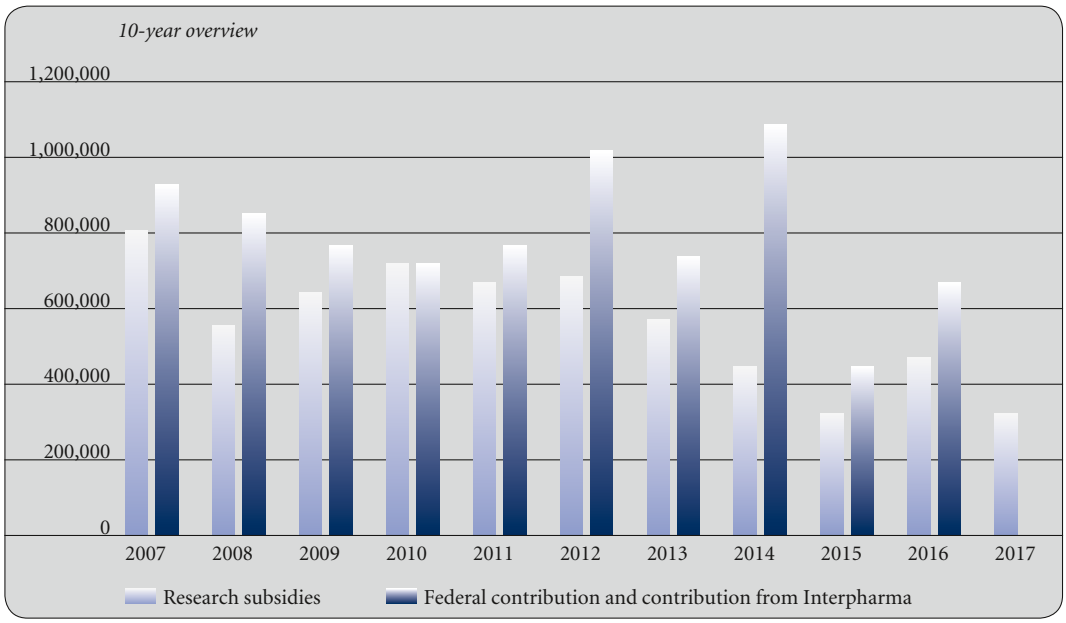
Financial business

Research funding for the 11 ongoing projects amounted to CHF 304,156.80 in 2017. The sum of CHF 2,000.– was used for participation in meetings where projects funded by the 3R Foundation were presented. Expenditure on project supervision and information (CHF 12,650.– + CHF 2,662.40) totalled CHF 15,312.40. Together with the balance of provisions for project funding (-CHF 304,156.10 = CHF 77,685.25 for provisions for 2018 minus CHF 381,841.35 liquidation of provisions for 2017), and the provision of CHF 8500.– for project supervision in 2018, total expenditure for research projects amounted to CHF 25,813.10. Administrative costs totalled CHF 54,056.70. With a provision of CHF 62,800.– for administrative costs for 2018, total expenditure therefore amounted to CHF 142,669.80.

On the income side, the equal financial commitment of the federal authorities and Interpharma has thus far constituted the basis for the Foundation's activities. The Foundation received no funding from the FSVO or from Interpharma in 2017, which meant that income was zero.

The balance therefore shows an excess of expenditure over income of CHF 142,669.80. This amount appears as a withdrawal of funds against capital funds on the balance sheet. Consequently, capital funds or unused research funding fell from CHF 236,235.52 at the end of 2016 to CHF 93,565.72 at the end of 2017.

At the end of the year under review the sum earmarked by the Administrative Board on the basis of project approvals but as yet not paid out amounted to CHF 77,685.25. This amount is fully covered by provisions. Consequently, as at 31.12.2017, there remained no contingency commitments that are not shown in the financial statements.



The budget for 2018 includes CHF 77,685.25 for ongoing projects.

Overview of grants awarded between 1987 and 2017

Together the federal authorities and Interpharma have contributed CHF 23,826,000.– to the Foundation since 1987. At the end of 2017 a total of CHF 19,632,951.45 had been granted for projects and other subsidies, of which CHF 19,555,266.90 had been paid out so far. Expenditure for project evaluation and supervision amounted to CHF 2,329,800.08 and the accumulated administrative costs totalled CHF 2,018,566.37 (8.6% of total expenditure or 10.4% of grants paid).

Annual financial statements

Profit and loss account	*2017*	*2016*
Federal contribution	0.00	365,000.00
Interpharma contribution	0.00	250,000.00
Total income	*0.00*	*615,000.00*
Research grants	–306,156.80	–472,172.90
Reimboursement of research grants	0.00	0.00
Adjustment of reserves for research grants	304,156.10	–205,481.45
Project supervision and information	–15,312.40	–77,758.60
Adjustment of reserves for project supervision and information	–8,500.00	
Balance for current projects	*– 25,813.10*	*270,549.95*
Administrative costs	–54,056.70	–59,637.20
Adjustment of reserves for administrative costs	–62,800.00	
Intermediate balance	*– 142,669.80*	*210,912.75*
Financial income	0.00	61.60
Financial result	*0.00*	*61.60*
Allocation to capital funds	0.00	-210,974.35
Withdrawal from capital funds	142,669.80	
Balance	*0.00*	*0.00*
Balance as per 31 December	*2017*	*2016*
Assets		
Liquid assets	249,270.97	620,632.57
Accounting apportionment assets	0.00	1,778.80
Current assets	*249,270.97*	*622,411.37*
Liabilities		
Accounting apportionment liabilities	5,720.00	3,334.50
Reserves for expenditure in 2018	148,985.25	381,841.35
Borrowed capital	*154,705.25*	*385,175.85*
Capital		
– Carried forward 1 January	236,235.52	25,261.17
– Adjustment of capital funds	–142,669.80	210,974.35
Balance as at 31 December	*93,565.72*	*236,235.52*
Foundation's capital	1,000.00	1,000.00
Organisational capital	**94,565.72**	**237,235.52**
	249,270.97	***622,411.37***

Contingency liabilities

None.

Münsingen, 23 February 2018

3R RESEARCH FOUNDATION

The Chairman sig. Joachim Eder

The Administrator sig. Ernst P. Diener

Auditors' report to the Administrative Board

DieWirtschaftsprüfer.ch AG in Thun audited the financial statements for the year according to standards of limited auditing and did not find any indication that the accounts and statements do not correspond to current legislation or the principles and regulations of the Foundation.

3R-Info Bulletins

In 2017 no new 3R-Info Bulletins were published and added to the Foundation's website (www.forschung3r.ch/en/publications/index.html).

List of Projects

A complete list of projects with summaries of each can be found on the Foundation's website (http://www.forschung3r.ch/en/projects/index.html).

List of current projects and those completed in 2017

122/10 Dr. Helene Rohrbach
Department of Clinical Veterinary Medicine, University of Berne
Improved perioperative analgesia and reduced stress during recovery for the experimental animal: ultrasound-guided sciatic and femoral nerve block in sheep and quantitative assessment of block quality

135/13 Dr. Benedikt Weber
Swiss Centre for Regenerative Medicine, University Hospital Zürich, Switzerland
In vitro engineering of a human cell-based three-dimensional dynamic model of atherosclerosis
Completed in 2017

136/13 Prof. Joachim Frey
Institute of Veterinary Bacteriology, Vetsuisse Faculty, University of Berne, Switzerland
Development of an in-vitro potency assay for Clostridium chauvoei vaccines: Replacement of the guinea-pig-challenge potency test

139/14 Dr. Marietta Herrmann
AO Research Institute Davos, Switzerland
A new in vitro microvascular model of the endothelial barrier
Completed in 2017

140/14 Dr. Marianne Schmid Daners
Institute for Dynamic Systems and Control, Zurich Federal Institute of Technology, Switzerland
Hydrocephalus simulator for testing of active ventriculoperitoneal shunts
Completed in 2017

141/14 Prof. Helmut Segner
Centre for Fish and Wildlife Health, University of Berne, Switzerland
In-vitro alternatives to in vivo bioconcentration testing with fish: restricted to rainbow trout or broadly applicable?
Completed in 2017

142/14 Prof. Christian de Geyter
University Hospital Basle, Switzerland
Validation of human stem-cell pluripotency using a bioreactor-based culturing system instead of a murine model to effect the development of embryoid bodies into teratomas

143/15 Prof. Olivier Guenat
ARTORG Centre, Lung Regeneration Tech, University of Berne
An advanced in-vitro model of pulmonary inflammation based on a novel lung-on-chip technology

144/15 Prof. Curzio Rüegg
Department of Medicine, Chair of Pathology, University of Fribourg
Development of in-vitro three-dimensional multi-cellular culture models to study the role of heterotypic cellular interactions in colorectal cancer invasion

145/15 Prof. Kristin Schirmer
EAWAG, Dübendorf
Combining computational modelling with in-vitro cellular responses in order to predict chemical impact on fish growth

146/15 Dr. Gerasimos Sykiotis
Endocrinology, Diabetology and Metabolism Service, Vaud University Hospital, Lausanne
Validation of a novel cell-based approach to study thyroidal physiology: Reduction and/or replacement of experiments with rodents

Office | Südstrasse 1 | P.O. BOX 1372
CH-3110 Münsingen | Switzerland
Phone 031 722 08 30 | Fax 031 722 08 34 | secretary.3r@bluewin.ch | www.forschung3r.ch